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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/670,004	09/25/2003	Kazuhiro Aikawa	Q77153	6236

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EXAMINER	
KISHORE, GOLLAMUDI S	
ART UNIT	**PAPER NUMBER**
1615	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/670,004	AIKAWA, KAZUHIRO	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 11-28-06
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment dated 11-28-06 is acknowledged.

Claims included in the prosecution are 1 and 4-6.

In view of the amendments, the 102 rejections of claims over Male-Brune (5,660,855) and GB are withdrawn.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1 and 4-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a specific benzimidazole derivative (compound 25 in example 2), does not reasonably provide enablement for active ingredient (claim 1) or benzimidazole derivative (claim 2). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The terms, 'active ingredient' and 'benzimidazole derivative' encompass multitudes of compounds and instant specification does not provide adequate support for the broadly recited terms. In Example 2 of the specification, applicant uses a specific compound without even specifying its chemical name and referring to it as only compound 25. Broad claims must have broad basis of support in the specification; in the absence of such support, claims must be limited to the specific compound used in the example.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that at page 4, lines 8-13, the specification describes that benzimidazole derivatives are well known in the art as evidenced by JP unexamined publications and a WO 95 reference. This argument is not persuasive since 'benzimidazole derivative' as used in the claims is a broad terms and instant specification does not specifically disclose specific compounds with chemical names or structures which could be used in practicing the invention; as pointed out before, the term encompasses multitudes of compounds and applicant has not shown the applicability of the invention to these multitudes of compounds.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 1 and 4-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear as to what applicant intends to convey by 'suppressing action on foaming of macrophages'.

Applicant cancels the original claim 2 reciting this expression and introduces the limitation in claim 1. Therefore, the rejection is applicable to claim 1 and its dependent claims. Applicant once again argues that the specification defines the benzimidazole derivative having suppressing action on foaming of macrophages as those disclosed in Japanese unexamined publications. This argument is not persuasive since the issue

here what the foaming of microphages means. Instant specification does not provide a definition of the term.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1 and 4-6 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 0 583 665 of record.

EP discloses liposomes containing a benzimidazole derivative. The phospholipids used are PC and PS in a molar ratio of 1:1 (abstract and page 33).

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that EP fails to disclose preparing the liposomes so that the liposome contains the benzimidazole compounds thereof and that the pharmaceutical test discloses that the test compounds and liposomes are added separately to the cultures of macrophages. This argument is not found to be persuasive since instant claims are composition claims and not method of preparation claims and the examiner has already cited the references of US 6,645,522 (col. 2, lines 50-52), US 6,348,214 (COL. 6, LINES 1-5) and (WO 97/25560 (page 7, lines 13-23) which show that the incubation of liposomes with the active agent results in the association of the active agent with the liposomal membrane are cited as interest. Applicant has not

shown that the benzimidazole in EP is not associated with the liposome membrane under the incubation conditions.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1 and 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0583 665 cited above in view of Aikawa (7,101,532) or Kitaguchi (7,008,614) or Schmidt (6,077,529) individually or in combination.

EP as discussed above teaches liposomes containing PC and PS in 1:1 molar ratio. The benzimidazole however, is added to the medium containing the liposomes. According to EP the benzimidazole derivatives are for the treatment of hyperlipidemia and arteriosclerosis.

Aikawa, and Kitaguchi while disclosing liposomal compositions for radiography of a vascular disease (atherosclerosis) teach that liposomes are selectively taken up by vascular smooth muscle cells and macrophages. The liposomes contain PC and PS in 1:1 molar ratio (abstract, Examples 5, 68 and 9 of Aikawa; abstract, Examples 4, 5 and 8 of Kitaguchi).

Schmidt discloses that liposomes containing are useful in handling arteriosclerosis. The phospholipids, which could be used in making the liposomes, include PC and PS (abstract, col. 5, lines 24-34 and claim 4).

Assuming that the benzimidazole derivatives of EP are not associated with the liposomal membrane: it would have been obvious to one of ordinary skill in the art to encapsulate or associate the benzimidazole derivatives of EP in liposomes since the references of Kitaguchi, and Aikawa each teach that the liposomes are selectively taken up by vascular smooth muscle cells and macrophages and since the reference of Schmidt teaches that liposomes can be used in handling atherosclerosis.

8. Claims 1 and 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aikawa (5,387,600) of record in view of Aikawa (7,101,532) or Kitaguchi (7,008,614) or Schmidt (6,077,529) individually or in combination.

Aikawa (600) teaches that benzimidazole derivatives for the treatment of atherosclerosis (abstract and claims). What is lacking in Aikawa is the use of liposomes as the carriers.

Aikawa, and Kitaguchi while disclosing liposomal compositions for radiography of a vascular disease (atherosclerosis) teach that liposomes are selectively taken up by vascular smooth muscle cells and macrophages. The liposomes contain PC and PS in 1:1 molar ratio (abstract, Examples 5, 68 and 9 of Aikawa; abstract, Examples 4, 5 and 8 of Kitaguchi).

Schmidt discloses that liposomes containing are useful in handling arteriosclerosis. The phospholipids, which could be used in making the liposomes, include PC and PS (abstract, col. 5, lines 24-34 and claim 4).

It would have been obvious to one of ordinary skill in the art to encapsulate or associate the benzimidazole derivatives of Aikawa (600) in liposomes since the

references of Kitaguchi, and Aikawa each teach that the liposomes are selectively taken up by vascular smooth muscle cells and macrophages and since the reference of Schmidt teaches that liposomes can be used in handling atherosclerosis.

The reference of Hope (6,139,871), which teaches the use of liposomes for the treatment of atherosclerosis, is cited of interest.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Woodward Michael can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/G S Kishore/

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK